SYNTHESIS AND CHARACTERISATION OF MULTI-FERROCENYL COMPOUNDS CONTAINING ENONE MOIETIES

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ORISSA-769008

CERTIFICATE

This is to certify that the dissertation entitled " **Synthesis and characterisation of multi-ferrocenyl compounds containing enone moeities"** being submitted by **Annu Kumari Pandey** to the **Department of Chemistry, National Institute of Technology, Rourkela, Orissa**, for the award of the degree of Master of Science is a record of bonafide research carried out by her under my supervision and guidance. To the best of my knowledge, the matter embodied in the dissertation has not been submitted to any other University / Institute for the award of any Degree or Diploma.

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I am grateful to **NIT ROURKELA** for giving me the permission and facility to do this project. I also acknowledge with a deep sense of reverence, my gratitude towards my parents and member of my family, who has always supported me, no matter what.

DECLARATION

I, **Annu Kumari Pandey**, hereby declare that the dissertation entitled **"Synthesis and characterisation of multi-ferrocenyl compounds containing enone moeities"** is the original work carried out by me under the supervision of **Dr. Saurav Chatterjee**, Department of Chemistry, National Institute of Technology, Rourkela and the present work or any part of this work has not been presented in any other University or Institute for the award of any other degree to the best to my belief.

Annu Kumari Pandey

ABSTRACT

Ferrocene based organometallic compounds have received intense attention in synthetic chemistry due to their increasing interest in biological, optical, and electrochemical properties. Among them, compounds containing heterocycles linked to ferrocene moiety have predominantly attracted importance because of their application in medicinal and materials chemistry. Recently, ferrocene incorporation into several drug compounds have improved the activity of the drug showing their potential in the field of medicinal chemistry. Ferrocene substituted tamoxifen and ferrocenyl chloroquine derivatives are among the many examples where the compound showed higher activity compared to their organic analogue. In view of their interesting properties and emerging potential, we focused our studies on the synthesis of ferrocene based chalcones and study of their biological, electrochemical and sensing properties. Chalcones itself constitute an important class of compounds with varied biological activities such as anti-cancer, anti-microbials, anti-malarial and anti inflammatory and are prime precursors to different types of heterocyclic compounds. Therefore, we chose to prepare a number of ferrocenyl chalcones and understand their electrochemical and biological properties.

CONTENTS

CHAPTER 1

INTRODUCTION

1.1 Ferrocene

Organometallic chemistry leaped forward in the early 1950s when the structure of ferrocene,$Fe(C_5H_5)_2$ was elucidated. It was the first of many complexes came to be known as metallocene, a name which arose because they precipitated in reactions similar to those of aromatic molecules. Ferrocene has a ferrous ion (Fe^{2+}) coordinated to two cyclopentadienyl (Cp) rings. The d-orbitals on Fe^{2+} are coordinated into the π orbitals on the two cyclopentadienyl radicals to form a unique sandwich structure. It is stable to high temperatures and unaffected by water, strong acids and alkalis. The unique stability of ferrocene is attributed to the distribution of 18 π electrons in the e_{2g} and a_{1g} non bonding molecular orbitals (Fig. 1).

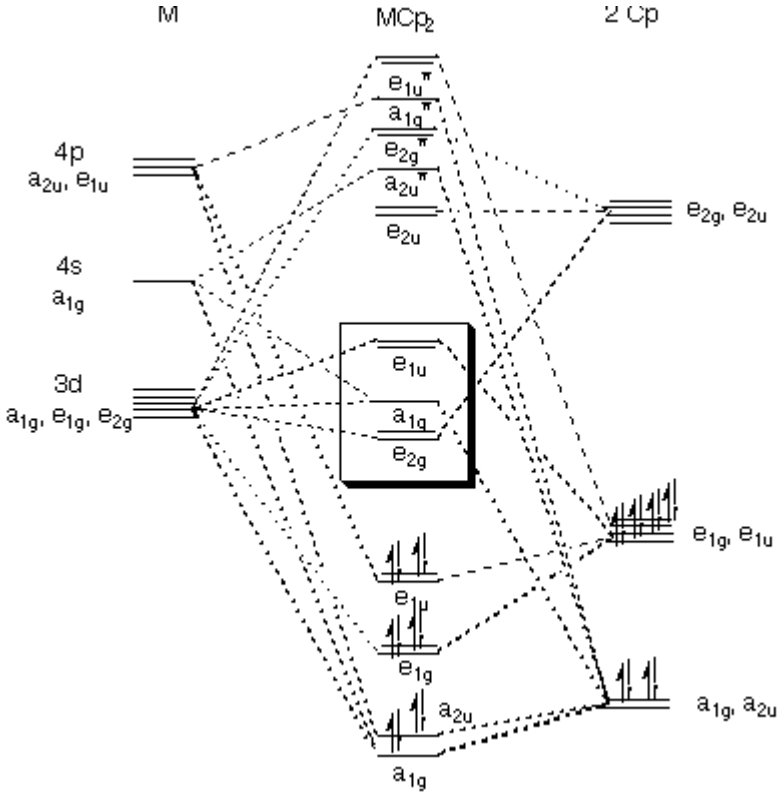


Fig 1.

The carbon-carbon bond distances are 1.40 Å within the five-membered rings, and the Fe-C bond distances are 2.04 Å. Although X-ray crystallography (in the monoclinic space group) points to the Cp rings being in a staggered conformation, it has been shown through gas

phase electron diffraction and computational studies that in the gas phase the Cp rings are eclipsed. The staggered conformation is believed to be most stable in the condensed phase due to crystal packing. The point group of the staggered conformation is D_{5d} and the point group of the eclipsed conformation is D_{5h}.Ferrocene behaves like an aromatic compound. It is susceptible to direct electrophilic substitution reactions, giving rise to a variety of substituted ferrocenes.

1.2. Chalcones

Chalcones (trans-1,3-diaryl-2-propen-1-ones) are natural products belonging to flavonoid, are considered as intermediate in the flavonoids biosynthesis, and are widespread in plants. The existence of the α,β-unsaturated ketone moiety in chalcones is a common part found in a large number of biological active compounds. Therefore, chalcone derivatives from nature or synthetic origin show diverse pharmacological activities, such as antimicrobial, antitumor, anticancer, radical scavenger, and inhibitor of topoisomerase. Beside, its immense usage in medicinal chemistry, it also have potential as artificial sweeteners, novel drugs and agrochemicals. To add to its usefulness, chalcone derivatives have various optical applications including second harmonic generation materials in non-linear optics, photorefractive polymers, holographic recording materials and fluorescent probes for sensing of metal ions.[1] Several heterocyclic ring compounds like pyrazole, pyrimidines with significant biological activity are synthesis from chalcones.[2] When chalcone substitutes the one or both aromatic group of ferrrocene and are connected by a enone bridge, gives an important class of compound called Ferrocenyl chalcone. Recent research in organomettalllic chemistry have been focussed on synthesis of ferrocenyl chalcones and their derivatives which shows marked electrochemical and biological properties.[3,4] Due to immense applications of chalcone makes it an important class of naturally occurring flavonoids exhibiting a broad spectrum of biological activities such as anti-cancer, anti-microbial, anti-malarial and anti-inflammatory activities.

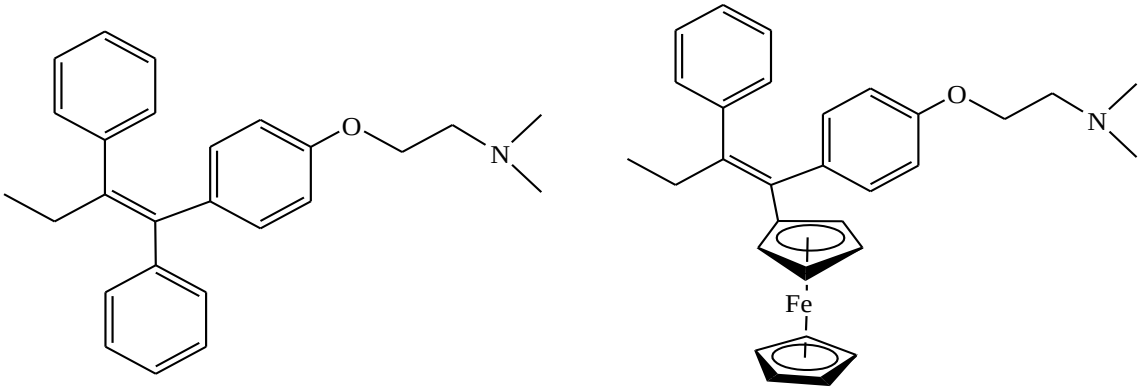
1.3. Application of ferrocene and its derivatives:

Ferrocene itself is nontoxic compound, has good redox property. It is an anti-aenemic or cytotoxic agent. Ferrocene-containing nucleic acids has been reported to be used in glucose biosensors and bioelectronics[5]. Detail applications of ferrocenyl derivatives are as follows:

1.3.1 MEDICINAL APPLICATIONS OF FERROCENE DERIVATIVES:

a. Anticancer Activity

Ferrocenyl derivatives have revolutionized the field of cancer research by being a very potential anticancer compound. Cancer is a class of disease characterized by uncontrolled cell proliferation and the ability of these cells to invade other tissues. It can be treated by methods including chemotherapy, which is one of the widely used strategies in the fight of cancer. Many ferrocenyl derivatives show good results as antitumor agents and some of them are now in clinical trials. Ferrocifen is more active than tamoxifen[6] (Fig. 2.)

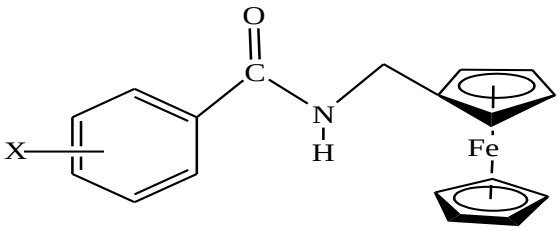


Tamoxifen
1

Ferrocifen
2

Fig 2.

Kenny et al., reported a series of N-(ferrocenylmethyl)benzene-carboxamide derivatives **(3)** which shows cytotoxic effects on the MDA-MB-435-S-F breast cancer cells.[7](Fig. 3.)



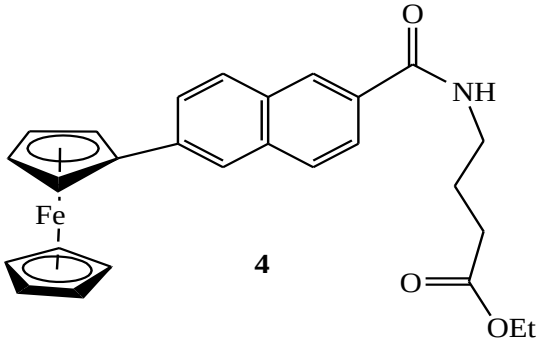
X=H,4-F,2-F,6-F

N-(ferrocenylmethyl)fluorobenzene-carboxamide derivatives

3

Fig. 3.

According to Kenny's and Simenel's groups N-(6-ferrocenyl-2-naphthoyl)-g-aminobutyric acid ethyl ester (**4**) and 1-N-ferrocenylmethyl thymine (**5**) are more active on human lung carcinoma cell line H1299 and carcinoma 755 respectively.[8-14] The anti-cancer activity of ferrocenyl derivatives of retinoids toward human lung cancer cell line (A549), human liver cancer cell line (BEL7404), and human tongue cancer cell line (Tca) exhibited higher than the parent 13-cis-retinoic acid,[15-17](Fig. 4.)



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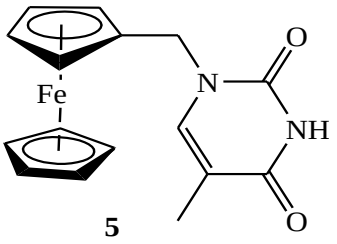
N-(6-ferrocenyl-2-naphthoyl)-g-aminobutyric acid ethyl ester



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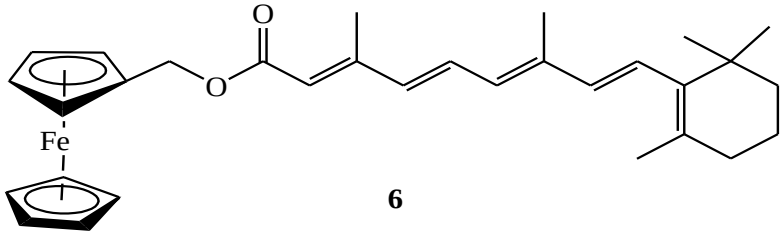
1N-ferrocenylmethyl thymine



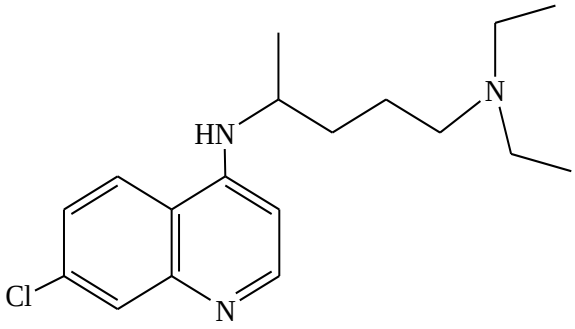
6

Retinoyl derivative of ferrocene

Fig. 4.

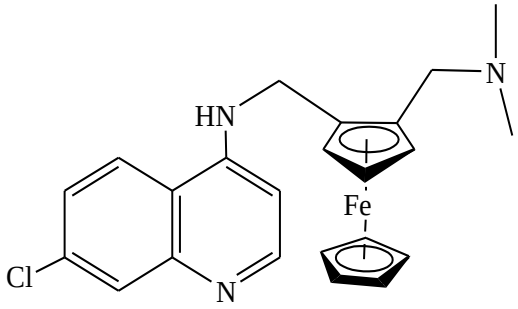
b. Antimalarial activity

Chloroquine (**7**) has long been used in treatment of malaria cause by Plasmodium falciparum, P. malariae. Ferrocene derivative of chloroquine, Ferroquine (**8**) and its derivatives (**9**) are found to be extremely active against CQ-susceptible and CQ-resistant *Plasmodium falciparum*.[18](Fig. 5.)



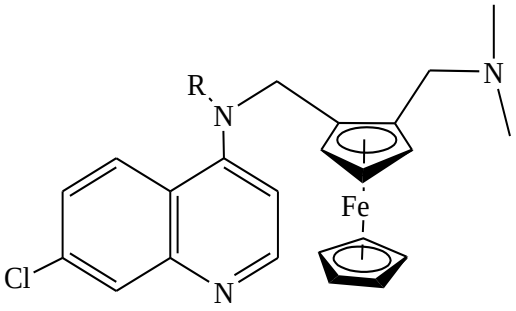
Chloroquine

7



Ferroquine

8



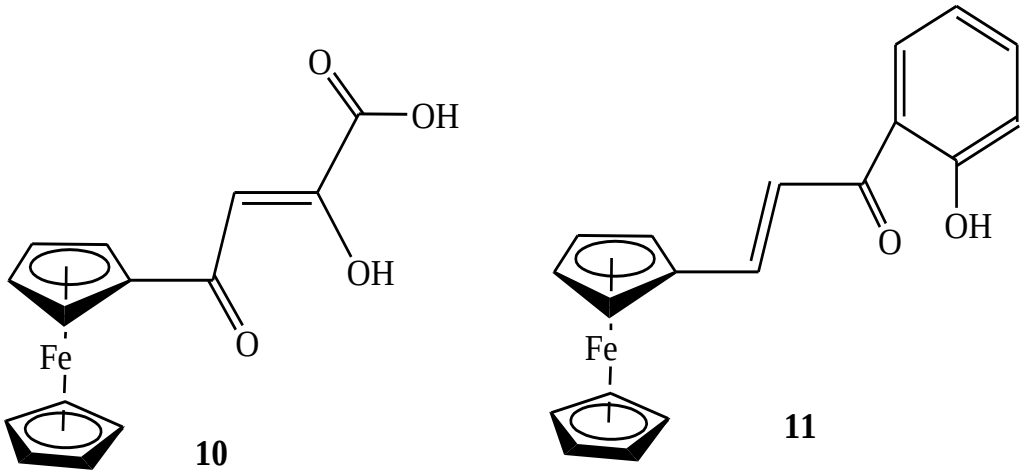
R= Me, Et, Pr, Bu,iBu

9

Fig. 5.

c. Anti-HIV Agent

Lately,HIV-1 integrase (IN) has emerged as an important therapeutic target for the design of anti-HIV agents because IN catalyzes the insertion of HIV proviral DNA into the host genome. Among the diverse structural classes of IN inhibitors, the β-diketo acid class of compounds has shown selective IN inhibition. For many of these compounds, complexation with boron difluoride increases their potency and selectivity towards IN inhibition. Ferrocenyl chalcones, ferrocenyl-2-hydroxy-4-oxo-2-butenoic acid (**10**) and hydroxyferrocene chalcone (**11**) has shown showed potent strand transfer inhibition.[19] (Fig. 6)

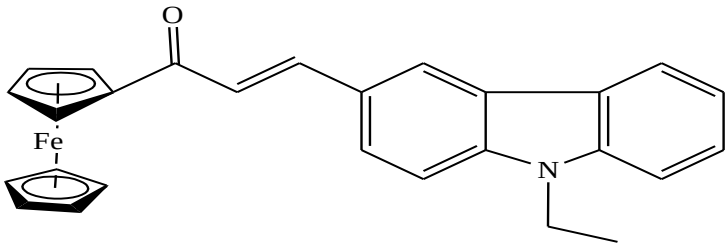


Some ß-diketo acids studied as potential HIV-1 integrase inhibitors

Fig. 6.

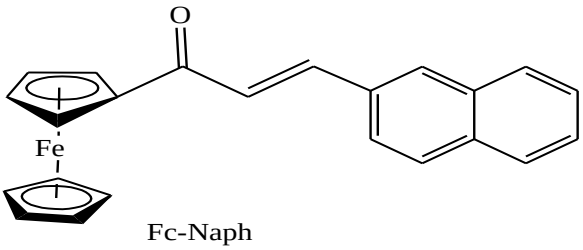
1.3.2 ***FLUORESCENCE PROPERTY:***

Ferrocenyl moiety connected with different fluorescent molecule show interesting fluorescence behavior, sometime it acts as auxochrome but some cases it act as quencher. For example in compound **Fc-EtCbz** (**13**) it act as auxochrome but in compounds **Fc-Naph** (**14**) and **Fc-Anth** (**15**) ferrocenyl moiety behaves as a fluorescence quencher.[20] (Fig. 7.)



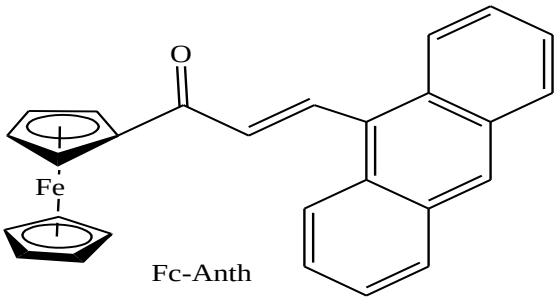
Ferrocenyl chalcones with N-ethyl carbazole(**Fc-EtCbz**)

13



Fc-Naph

14



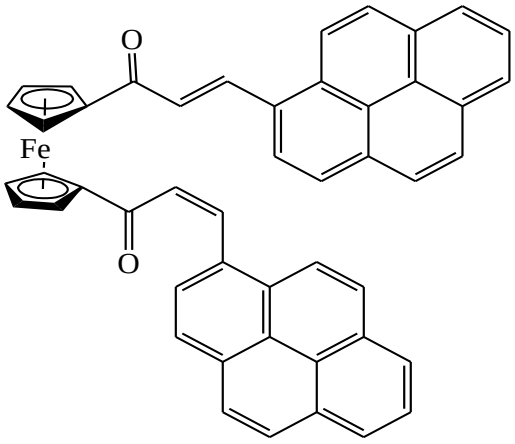
Fc-Anth

15

Fig. 7.

1.3.3 ***CHEMO SENSOR PROPERTIES***:

There are some reported ferrocene based organometallic compounds which have sensing property toward a particular ion. Lee et al. have reported ferrocenyl chalcones linked with two pyrene moieties **(16)** highly selective toward Fe(III) ions over Fe(II) ions.[21](Fig. 8.)



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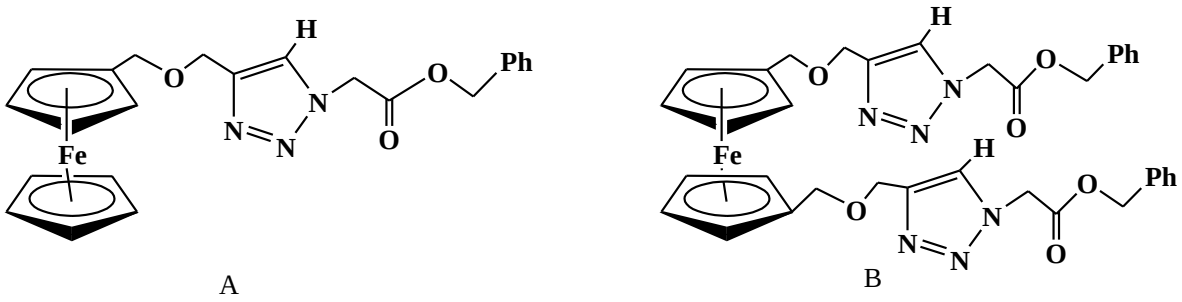
Ferrocenyl chalcones with di-1-pyrene

Fig. 8.

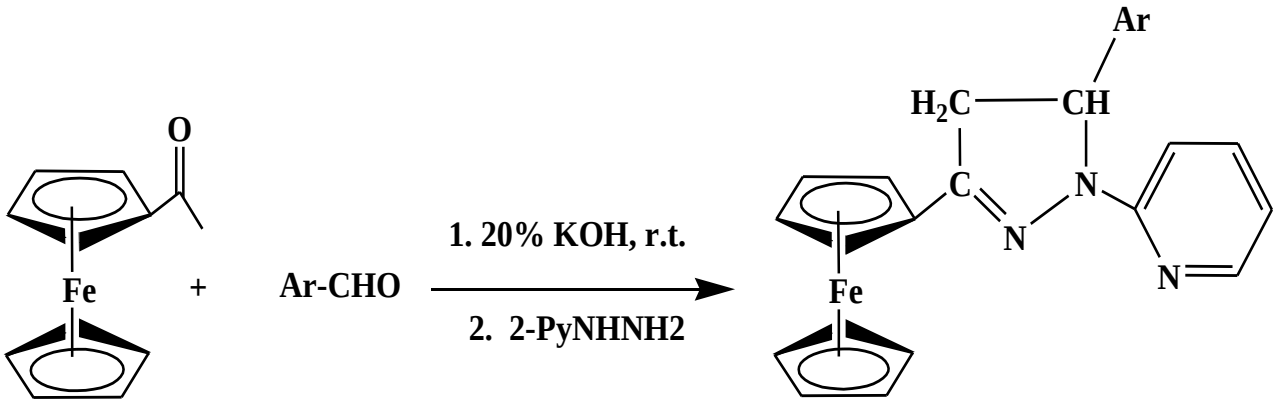
Recently, Thakur and coworkers[22] have reported the electrochemical, optical, and cation-sensing properties of two synthesized triazole-tethered ferrocenyl benzylacetate derivatives (Fig. 9) which can be used for the selective colorimetric detection of Hg^{2+} in an aqueous environment over $Ni^{+2}$and Cu^{2+} cations.



A B

Fig 9.

Trivedi *et. al.* have reported a simple one-pot synthesis, characterization, optoelectronic and cation sensing properties of 1-(2-pyridyl)-3-ferrocenylpyrazolines (scheme 1). These ferrocene compounds behave as selective multichannel chemosensors in the presence of $Co^{2+,}$ $Cu^{2+,}$ and Zn^{2+} ions. A maximum cathodic shift in the redox potential of the ferrocenium couple was observed towards the Co^{2+} ion, while a minimum shift was observed with the Zn^{2+} ion on complexation with this receptor.[23]



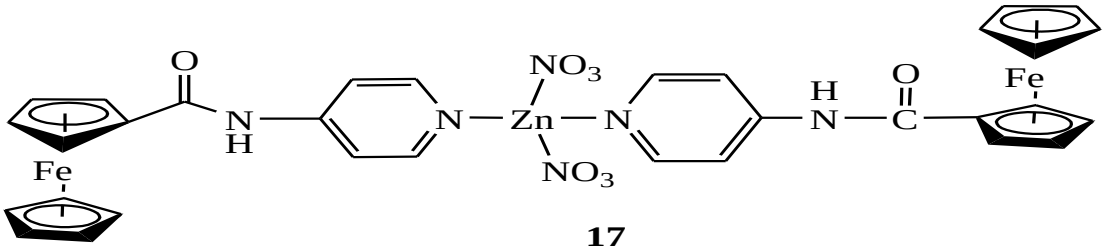
Ar= 1-napthyl, 9-anthryl, 1-pyrenyl

Scheme 1.

1.3.4. FERROCENE DERIVATIVES AS NON LINEAR OPTIC MATERIALS:

Nonlinear optics (NLO) is the branch of optics that describes the behavior light in nonlinear media, that is, media in which the dielectric polarization **P** responds nonlinearly to the electric field **E** of the light. This nonlinearity is typically only observed at very high light intensities (values of the electric field comparable to interatomic electric fields, typically 10^8 V/m) such as those provided by lasers. Above the Schwinger limit, the vacuum itself is expected to become nonlinear. In nonlinear optics, the superposition principle no longer holds. Nonlinear optics remained unexplored until the discovery of Second harmonic generation shortly after demonstration of the first laser. (Peter Franken *et al.* at University of Michigan in 1961). Second -order NLO materials is used in laser industry and Third-order NLO materials can be used for a number of photonic applications, for example, optical signal processing, optical communication, optical computing, electro-optic modulation.

Ferrocene-containing molecules with nonlinear optical (NLO) properties are currently attracting a great deal of attention. Hou.et.al[24] have synthesized ferrocenyl ligands [(4-pyridylamino)-carbonyl]ferrocene(4-PFA) and 1,1-bis[(4-pyridylamino)-carbonyl]ferrocene (4-BPFA), and their corresponding complexes[Zn(4-PFA)$_2$(NO_3)2](H_2O) (**17**), [Hg_2(OAc)$_4$(4-BPFA)$_2$](CH_3OH) (**18**),which are potential third –order NLOs.(Fig. 10.)



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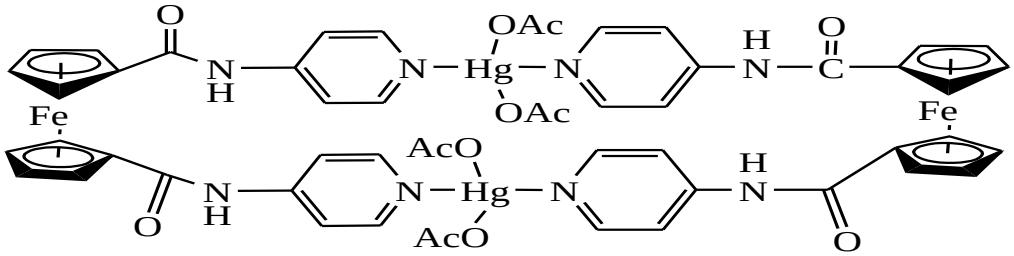

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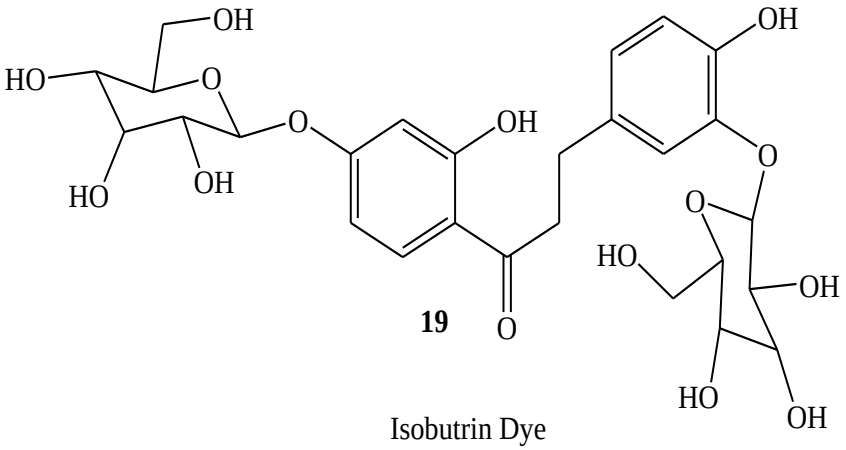
Fig. 10.

1.3.5. FERROCENYL AND CHALONE DERIVATIVES AS SOLAR CELL COMPOUND

There has been considerable research in harnessing solar energy which is a renewable and clean source of energy for different applications such as dye-sensitized solar cells (DSSCs), photocatalysis, solar to-chemical conversion, etc., sensitizers with good optical properties over the visible range are essential.[25] A number of molecular sensitizers in the form of organic dyes (including heavy metal ion incorporated ones) have been synthesized and are being used, whose corresponding methods of synthesis, application and prolonged use are not eco-friendly. So focus has shifted to explore sources of new natural dye systems that are stable, nontoxic (biocompatible), and with the desirable optoelectronic properties.[29] There have been some interesting explorations of natural dyes in the context of the dye-sensitized solar cell (DSSC) application using pigments obtained from biomaterials such as flowers, fruits and leaves.[26-34] In this regard, Agarkar et al. have studied isobutrin (**19**) belonging to chalcone class, extracted from a natural flower source Butea Monosperma (Flame of the Forest) for possible use in dye sensitized solar cells as well as other optoelectronic applications. In DSSCs, purified isobutrin yields very promising solar conversion efficiency of 1.8%. [35] (Fig. 11.)



Isobutrin Dye

Fig. 11.

There are also some ferrocene derivatives those are studied as Dye-sensitized solar cell compounds.One of them is reported by Hong *et. al* .[36](Fig. 12.)

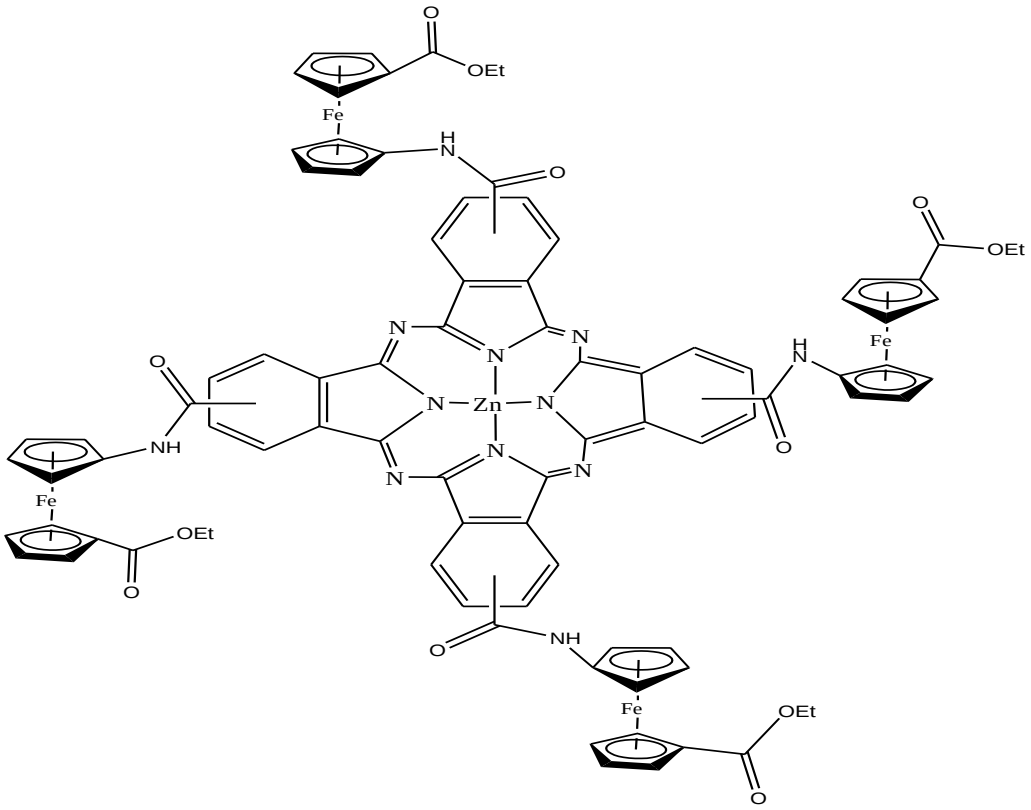


Fig. 12.

On the basis of the above literature survey we have been inspired to synthesize multi-ferrocenyl chalcones and their derivatives. We have been able to synthesize some multi ferrocenyl compounds and their derivatives and characterised using IR and NMR spectroscopic techniques. We will use these compounds for biological, electrochemical and photovoltaic study. The detail description of synthesis and characterisation is given in chapter 2.

CHAPTER 2

SYNTHESIS AND CHARACTERISATION OF FERROCENYL CHALCONES

2.1. Introduction

Recent research has been focused on the synthesis and characterizations of carbon chains linked with organometallic fragments and study their biological and materialistic properties. In view of the enormous research activity of organometallic compounds containing ferrocenyl and half sandwich moieties, we have been motivated to synthesize various compounds containing organic chains and multiple metal fragments and understand their biological, electrochemical and optical properties. Chalcone, a naturally occurring flavonoides is an antibacterial, anti-inflammatory and anticancer pharmacological agent and also have potential application as artificial sweeteners, novel drugs and agrochemicals. In addition, chalcone derivatives are widely used for various optical applications including second harmonic generation materials in non-linear optics, photorefractive polymers, holographic recording materials and fluorescent probes for sensing of metal ions. These are also widely used to prepare heterocyclic ring compounds like pyrazole, pyrimidines with significant biological activity. Ferrocenyl chalcone compounds belong to a chalcone family in which one or both the aromatic group is substituted by ferrocenyl unit and are connected by an enone bridge. Recently, a bunch of different ferrocenyl chalcones and their derivatives have been synthesized which shows marked electrochemical and biological properties[1]. These systems have been investigated as precursors for a large variety of ferrocene containing heterocycles like pyrazoles, pyrimidines etc[2]. It has now been well established that chalcone moieties constitute an important class of naturally occurring flavonoids and exhibit a wide spectrum of biological activities such as anti-cancer, anti-microbial, anti-malarial and anti-inflammatory activities. Recent investigation reveals their importance in biological studies which led to the immergence of a relatively new field of bioorganometallic chemistry [37]. A large number of ferrocene and half sandwich based compounds have been found to display interesting cytotoxic, DNA cleaving and other biological activities[3,4,38-41] . Ferrocene substituted tamoxifen and ferrocenyl chloroquine derivative are among the many examples where ferrocene incorporation have improved the activity of the drug[42]. Recently, our research group have reported some biologically active ferrocenyl and cymantrenyl hydrazone compounds and synthesized half-sandwich based dithiocarboxylato-alkyne complexes by sunlight driven reaction. Some of these organometallic compounds showed remarkable antibacterial properties[41].

2.2. Experimental Section

2.2.1 General Procedures

All reactions and manipulations were carried out under an inert atmosphere of dry, pre-purified nitrogen using standard Schlenk line techniques. Solvents were purified, dried and distilled under nitrogen atmosphere prior to use. Infrared spectra were recorded on a Perkin Elmer Spectrum RX-I spectrometer as dichloromethane solutions in 0.1 mm path lengths KBr cell and NMR spectra on a 400 MHz Bruker spectrometer in $CDCl_3$. HPLC grade dichloromethane is used for all spectroscopic analysis. TLC plates (20x20 cm, Silica gel 60 F254) were purchased from Merck. The compounds **3a**, **3b**, **4a** and **5a** was synthesized and characterized according to the procedure established by our research group.

2.2.2. Synthesis of $[Fe(\eta^5\text{-}C_5H_4CHO)_2]$ and $[Fe(\eta^5\text{-}(C_5H_5)(\eta^5\text{-}C_5H_4CHO)]$:

In a two necked round bottom flask, ferrocene (2 gm) **(1)** was taken with hexane (40ml) and was stirred in room temperature under nitrogen atmosphere. To this reaction mixture, n-butyl lithium (17ml) was added and left overnight. Then, DMF(1.8ml) and diethyl ether(8ml) was added and stirred for 1 hour in nitrogen atmosphere.Then,35% HCl(4ml) was taken in H_2O (27ml) and added to the reaction mixture and stirred for some time and then removed. The reaction was monitored by TLC. On completion of the reaction, the solution was dried under vacuum and the residue was dissolved in dichloromethane solvent and subjected to chromatographic work- up using preparative TLC. Pure dialdehyde and monoaldehyde ferrocene was separated through column chromatography.

2.2.3. Synthesis of $Fe(\eta^5\text{-}C_5H_4COCH_3)_2]$:

In a two necked round bottom flask, ferrocene (4 gm) (**2**) was taken with DCM (50ml) and stirred in room temperature under nitrogen atmosphere for 10 minutes to dissolve. Then, acetyl chloride (4ml) was added slowly and left for stirring for 15 minutes. After that, $AlCl_3$ (9.2gm) was added slowly and left for stirring for 4 hours. The reaction was monitored by TLC. Then, reaction mixture was poured in a beaker with ice cold water and extracted. On completion

of the reaction, the solution was dried under vacuum and the residue was subjected to chromatographic work using preparative TLC. Pure diacetyl and monoacetyl ferrocene was separated through column chromatography.

2.2.4. Synthesis Of $[(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4)C(O)CHCH(\eta^5\text{-}C_5H_4)Fe(\eta^5\text{-}C_5H_4)CHO]$:

A two necked round bottomed flask containing a ethanolic solution (10 ml) of $[Fe(\eta^5\text{-}C_5H_4CHO)_2]$ (**1a**) (21mg, 0.1 mmol) and $[(\eta^5C_5H_5)Fe(\eta^5\text{-}C_5H_4COCH_3)]$**(2b)** (0.1 mmol) was taken under inert atmosphere. Sodium hydroxide in ethanol solution was then added in excess to the reaction mixture and stirring was continued at room temperature under inert atmosphere for one hour and then subjected to vacuum for 30 minutes. The reaction was continuously monitored by TLC and on completion of the reaction the solution was dried under vacuum and the residue was dissolved in dichloromethane solvent and subjected to chromatographic work-up using column chromatography. The products were separated using ethylacetate/hexane (20:70 v/v) solvent mixture. (Scheme 3)

3a. IR(ν_{CO}, cm^{-1},CH_2Cl_2) 1683(vs), 1647 (vs), 1588(s). ^{1}H NMR (δ, $CDCl_3$): 4.25 (s, η^5-C_5H_5, 5H), 4.56 (t, η^5-C_5H_4, 2H), 4.61 (t, η^5-C_5H_4, 2H), 4.62 (t, η^5-C_5H_4, 2H), 4.68 (t, η^5-C_5H_4, 2H), 4.79 (m, η^5-C_5H_4, 4H), 4.91 (t, η^5-C_5H_4, 2H), 6.77 (d, ═C*H*, J = 15, 1H), 7.59 (d, C*H*═, J = 15, 1H), 9.95 (s, C*H*O, 1H).

3b. IR(ν_{CO}, cm^{-1},CH_2Cl_2) 1647 (vs), 1589(s)^{1}H NMR (δ, $CDCl_3$): 4.2(s, η^5-C_5H_5, 5H), 4.49 (t, η^5-C_5H_4, 4H), 4.54 (t, η^5-C_5H_4, 4H), 4.57 (t, η^5-C_5H_4, 4H), 4.01 (t, η^5-C_5H_4, 4H),

2.2.5. Reaction of [$(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4)C(O)CHCH(\eta^5\text{-}C_5H_4)Fe(\eta^5\text{-}C_5H_4)CHO$] with O-hydroxy acetophenone

Room temperature reaction was carried out with [$(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4)C(O)CHCH(\eta^5\text{-}C_5H_4)Fe(\eta^5\text{-}C_5H_4)CHO$] (**3a**) and o-hydroxy acetophenone **(4)** in ethanol solvent and in presence of excess ethanol. The reaction was stirred at nitrogen atmosphere for 16 hours and subjected to vacuum for 30 minutes. Reaction was continuously monitored using TLC. The product was isolated by preparative TLC using ethylacetate/pet.Ether solvent mixture. Preliminary observation of the product polarity (that is the solvent front at which it moves in TLC) reveals the tentative formation of the desired compound as shown in Scheme 4. Compound **(4a)** confirmation was done by IR and NMR spectroscopy.

4a. IR(ν_{CO}, cm^{-1},CH_2Cl_2) 1731(vs), 1632(vs), 1579(s)1564(s),3440(br) ,^{1}H NMR (δ, $CDCl_3$): 4.179 (s, η^5-C_5H_5, 5H), 4.5 (m, η^5-C_5H_4, 4H), 4.56(t, η^5-C_5H_4, 2H), 4.6 (m, η^5-C_5H_4, 4H), 4.75 (t, η^5-C_5H_4, 2H), 7.8 (d, ═C*H*, J = 15.6, 1H), 6.65 (d, C*H*═, J = 15.6, 1H), 7.6 (d, ═C*H*, J = 15.2, 1H), 7.18 (d, C*H*═, J = 16, 1H) 13.00 (s, OH, 1H).

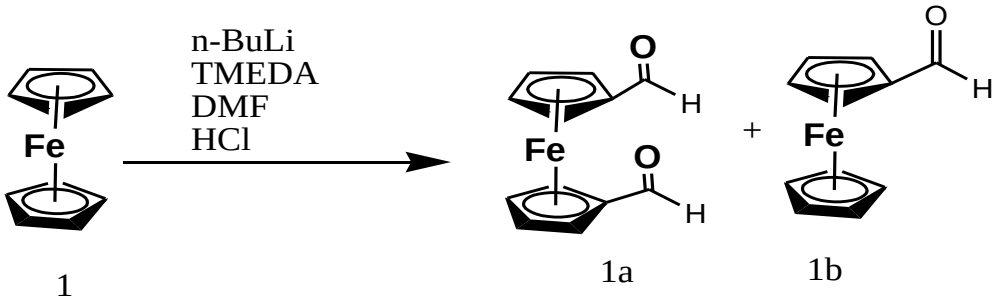
2.2.6. Reaction of [$(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4)C(O)CHCH(\eta^5\text{-}C_5H_4)Fe(\eta^5\text{-}C_5H_4)CHO$] with Acetone:

Room temperature reaction was carried out with [$(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4)C(O)CHCH(\eta^5\text{-}C_5H_4)Fe(\eta^5\text{-}C_5H_4)CHO$] (**3a**) and acetone (**5**) in ethanol solvent and in presence of excess ethanol. The reaction was refluxed at nitrogen atmosphere for 45 minutes and then vacuum to dry. Reaction was continuously monitored using TLC. The product was isolated by preparative TLC using ethylacetate/Pet.Ether solvent mixture. Preliminary observation of the product polarity (that is the solvent front at which it moves in TLC) reveals the tentative formation of the desired compound as shown in Scheme 5. The structural identity of compound **5a** confirmation was done by IR and NMR spectroscopy.

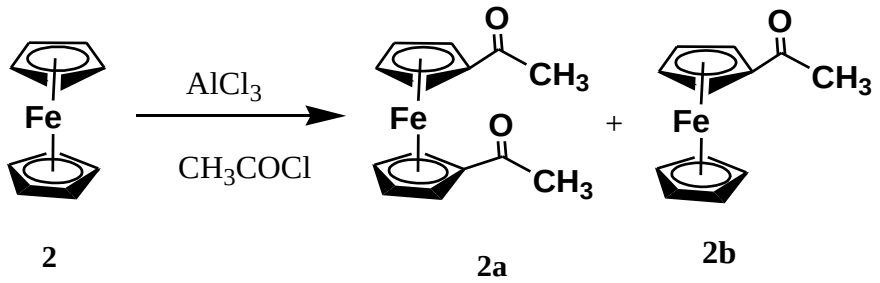
5a: IR (ν_{CO}, cm^{-1}, CH2Cl2) 1660(vs), 1650(vs), 1614(s), 1589(s). ^1H NMR (δ, $CDCl_3$): 5.319 (s, η^5-C_5H_5, 5H), 4.877 (t, η^5-C_5H_4, 2H), 4.599(t, η^5-C_5H_4, 2H), 4.573 (t, η^5-C_5H_4, 2H), 4.513 (t, η^5-C_5H_4, 2H), 4.465 (t, η^5-C_5H_4, 2H), 7.562 (d, ═C*H*, J = 15.6, 1H), 6.677 (d, C*H*═, J = 15.6, 1H), 7.29 (d, ═C*H*, 1H), 6.3 (d, C*H*═,1H), 2.233 (s, CH_3, 3H).

2.3. Results and discussion

All the starting materials Mono-aldehyde ferrocene (**1b**), Di-aldehyde ferrocene (**1a**), Mono-acetyl ferrocene (**2a**) and Di-acetyl ferrocene (**2b**) are synthesized using reported procedure and are confirmed from previous prepared compounds.



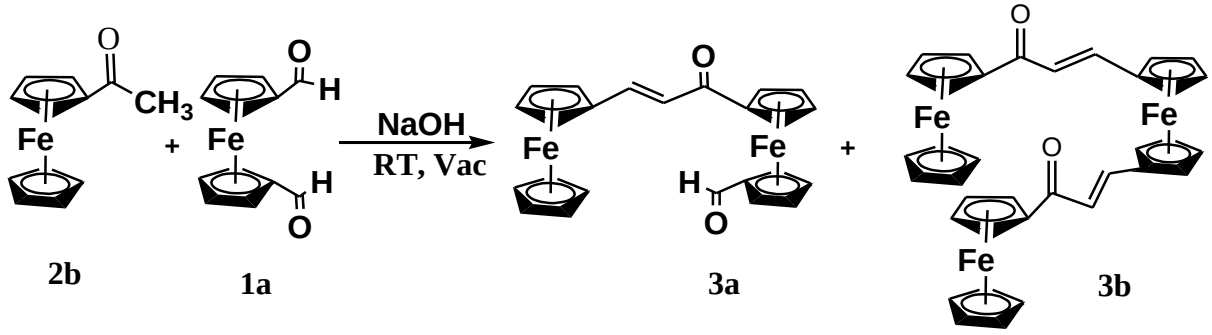
SCHEME 1.



SCHEME 2

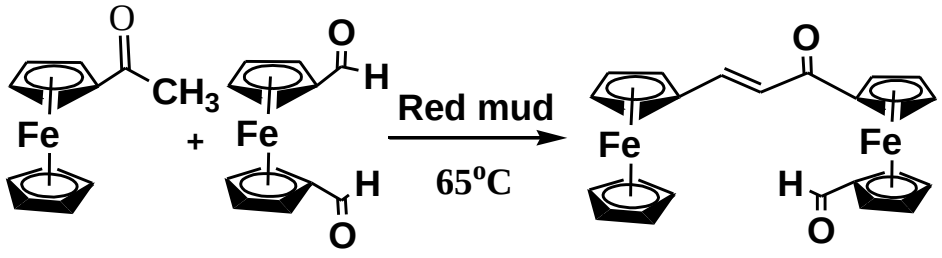
Synthesis of ferrocenyl chalcone derivatives **3a**, **3b, 4**a, **5**a, was carried out by modified Claisen-Schmidt condensation. Compound [(η^5-C_5H_5)Fe(η^5-C_5H_4)C(O)CHCH(η^5-C_5H_4)Fe(η^5-C_5H_4)CHO], **3a**,and ,[Fe_2(η^5-C_5H_4)$_4${(CHCH)C(O)}$_2$], **3b**, (scheme-3) were synthesized using sodium hydroxide in ethanol, 1 hour stirring and 5 min vaccum dry. required. The reaction times

were determined by monitoring the consumption of starting materials as indicated by TLC. The reaction time for the conventionally synthesized chalcones is more than 10 to 12 h, with very small yield while in modified procedure where vacuum is used it gives excellent yield within 5 to 10 minutes. The separation of **3a** and **3b** is difficult from the reaction mixture and yield of **3a** is less in this method, so a new procedure with red-mud (solid state synthesis, stirring at 65^0C for 7 hours) is employed to synthesize **3a** which gives excellent yield (scheme-4). The formation of **3a** is confirmed by IR and NMR in DCM and $CDCl_3$ where 1680 cm^{-1} and 1650 cm^{-1} are aldehyde C=O and α,β-C=O respectively in IR spectrum and δ, 4.25 (s, η^5-C_5H_5, 5H), 4.56 (t, η^5-C_5H_4, 2H), 4.61 (t, η^5-C_5H_4, 2H), 4.62 (t, η^5-C_5H_4, 2H), 4.68 (t, η^5-C_5H_4, 2H), 4.79 (m, η^5-C_5H_4, 4H), 4.91 (t, η^5-C_5H_4, 2H), 6.77 (d, ═C*H*, J = 15, 1H), 7.59 (d, C*H*═, J = 15, 1H), 9.95 (s, C*H*O, 1H) shows the di-ferrocenyl compound with a pendent aldehyde group. The **3b** compound is symmetrical and therefore 1644 cm^{-1} shows the presence of two α,β-C=O groups and δ, 4.2 (s, η^5-C_5H_5, 5H), 4.49 (t, η^5-C_5H_4, 4H), 4.54 (t, η^5-C_5H_4, 4H), 4.57 (t, η^5-C_5H_4, 4H), 4.01 (t, η^5-C_5H_4, 4H), shows the tri ferrocenyl symmetrical chalcone.



2b **1a** **3a** **3b**

SCHEME 3

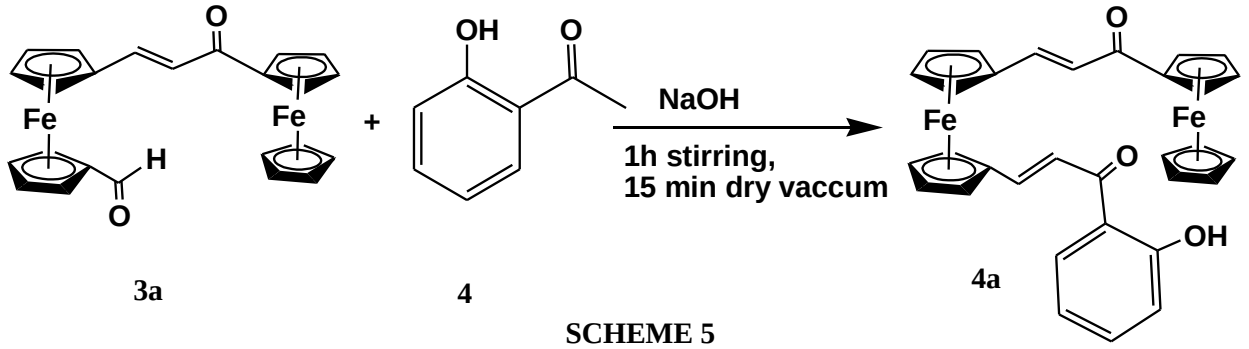


2b **1a** **3a**

SCHEME 4

Compound **4a** was synthesized from **3a** and **4** using sodium hydroxide in ethanol and 1 hour stirring and 15 min vacuum dry (scheme-5) . The reaction times were determined by

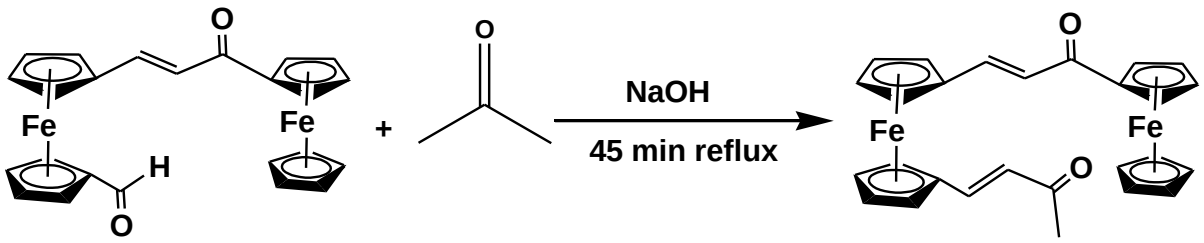
monitoring the consumption of starting materials as indicated by TLC. The product was separated using preparative thin layer chromatography with pet ether and ethyl acetate as solvent mixture. In IR 1731 cm^{-1}, 1632 cm^{-1}, 3440 cm^{-1} shows the presence of two carbonyl groups and the presence of –OH group respectively. In NMR δ, 4.179 (s, η^5-C_5H_5, 5H), 4.5 (m, η^5-C_5H_4, 4H), 4.56(t, η^5-C_5H_4, 2H), 4.6 (m, η^5-C_5H_4, 4H), 4.75 (t, η^5-C_5H_4, 2H) indicates the presence of ferrocenyl cp rings while 7.8 (d, ═C*H*, J = 15.6, 1H), 6.65 (d, C*H*═, J = 15.6, 1H), 7.6 (d, ═C*H*, J = 15.2, 1H) and 7.18 (d, C*H*═, J = 16, 1H) reveals the presence of olefinic protons and peaks at 13.00 (s, OH, 1H) shows the presence of OH protons. The IR and NMR spectral analysis reveals the formation of unsymmetrical di ferrocenyl chalcone (**3a)**.



3a **4** **4a**

SCHEME 5

Compound **5a** was synthesized from **3**a and **4** using sodium hydroxide in ethanol (scheme-6). The duration of the reaction was determined by monitoring the consumption of starting materials as indicated by TLC. The product was separated using preparative thin layer chromatography with pet ether and ethyl acetate solvent mixture. In IR spectrum shows bands at 1660 cm^{-1} and 1650 cm^{-1} region and indicates the presence of two carbonyl groups in the molecules. ^{1}H NMR shows ferrocenyl peaks at δ,5.32 (s, η^5-C_5H_5, 5H), 4.88 (t, η^5-C_5H_4, 2H), 4.6 (t, η^5-C_5H_4, 2H), 4.57 (t, η^5-C_5H_4, 2H), 4.51 (t, η^5-C_5H_4, 2H), 4.47 (t, η^5-C_5H_4, 2H) and peaks at 7.562 (d, ═C*H*, J = 15.6, 1H), 6.677 (d, C*H*═, J = 15.6, 1H), 7.29 (d, ═C*H*, 1H), 6.3 (d, C*H*═,1H) shows the presence of olefinic protons while methyl protons have been detected at 2.23 (s, CH_3, 3H) position. Spectroscopic analysis reveals the presence of unsymmetrically substituted ferrocenyl-chalcone with a pendent acetyl group.



3a **5** **5a**

SCHEME 6

2.4. *Conclusion:*

Multi-ferrocenyl chalcones with more than one ferrocene groups have been synthesized using condensation reaction and characterised by IR and NMR spectroscopy. The biological and electrochemical studies of the synthesized organometallic compounds are under investigation. Selective synthesis of ferrocenyl chalcones with pendant aldehyde and ketonic group have been carried out using redmud and has been used to prepare unsymmetrically substituted ferrocenyl compounds. These compounds can also be used to link different heterocyclic moieties and flouroscent units to get organometallic compounds with novel properties.

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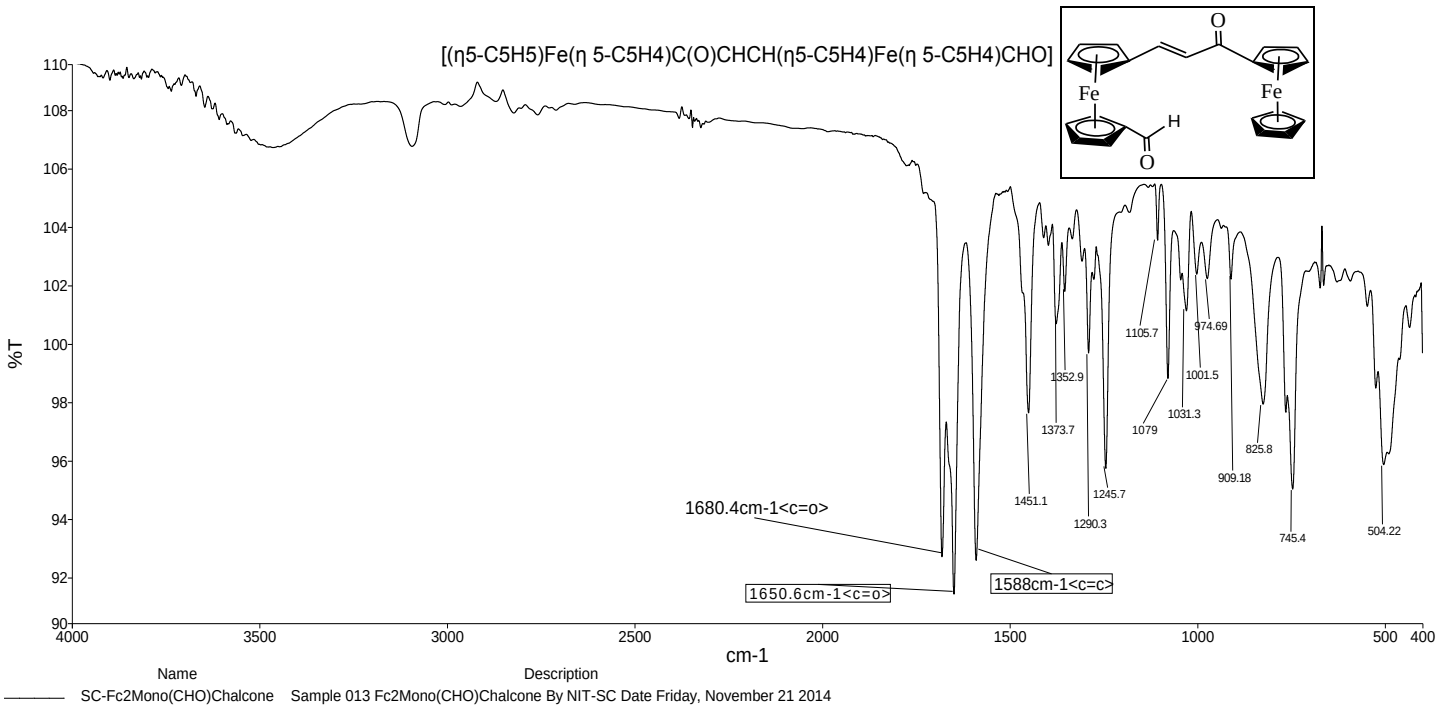
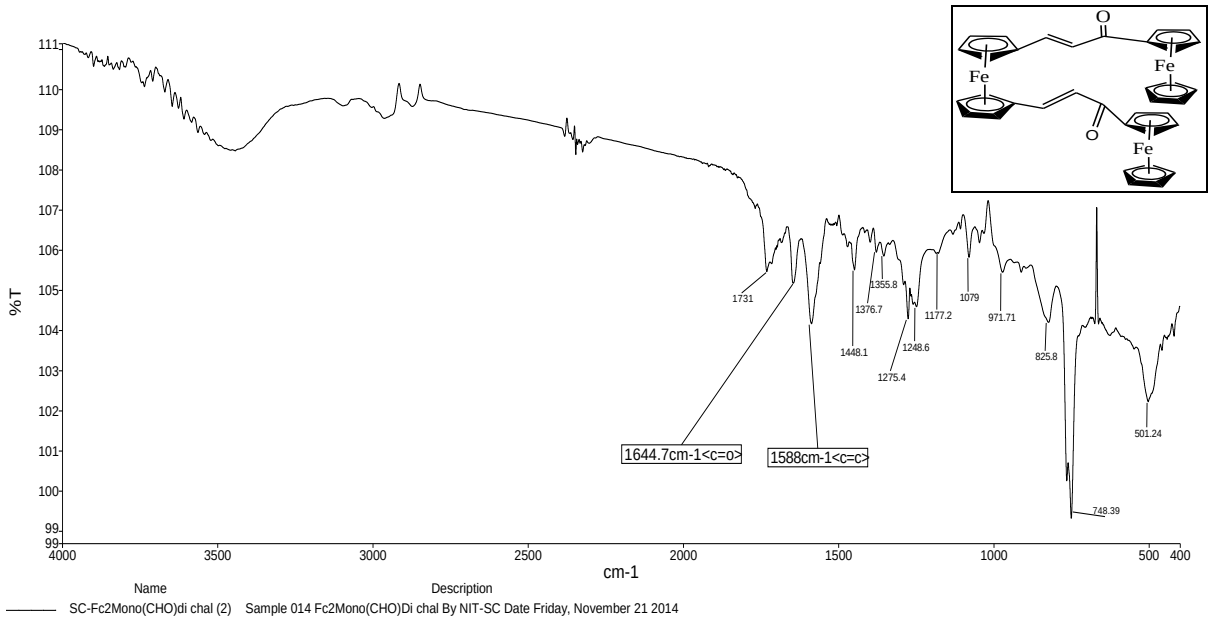
4. ANNEXURE 1:

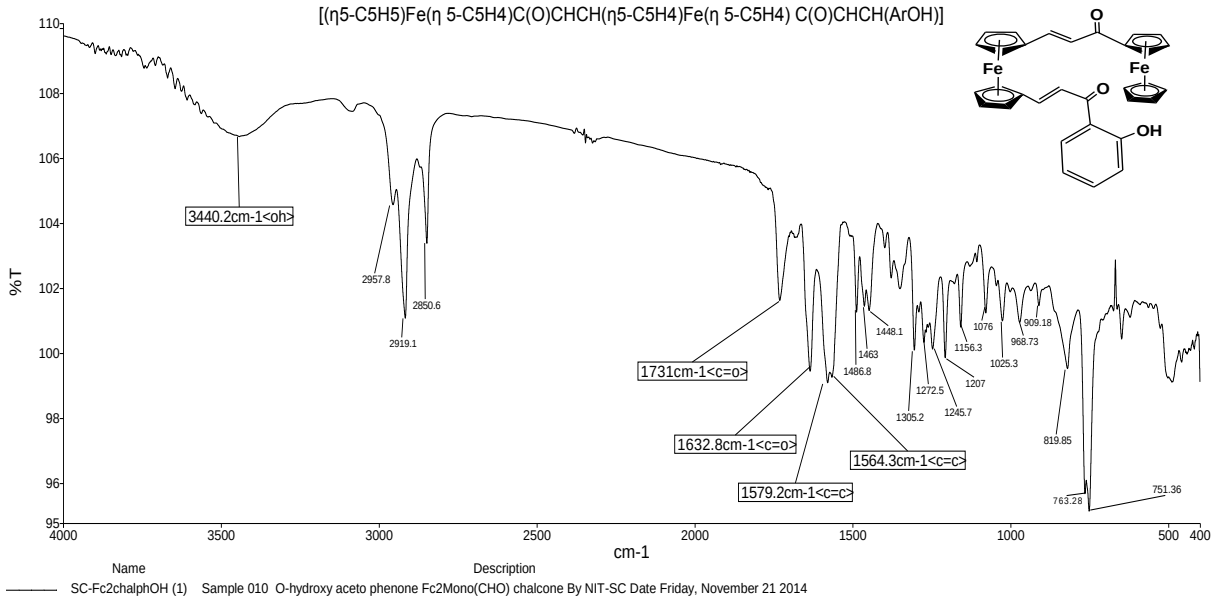
a)IR OF [(η5-C5H5)Fe(η 5-C5H4)C(O)CHCH(η5-C5H4)Fe(η 5-C5H4)CHO]:



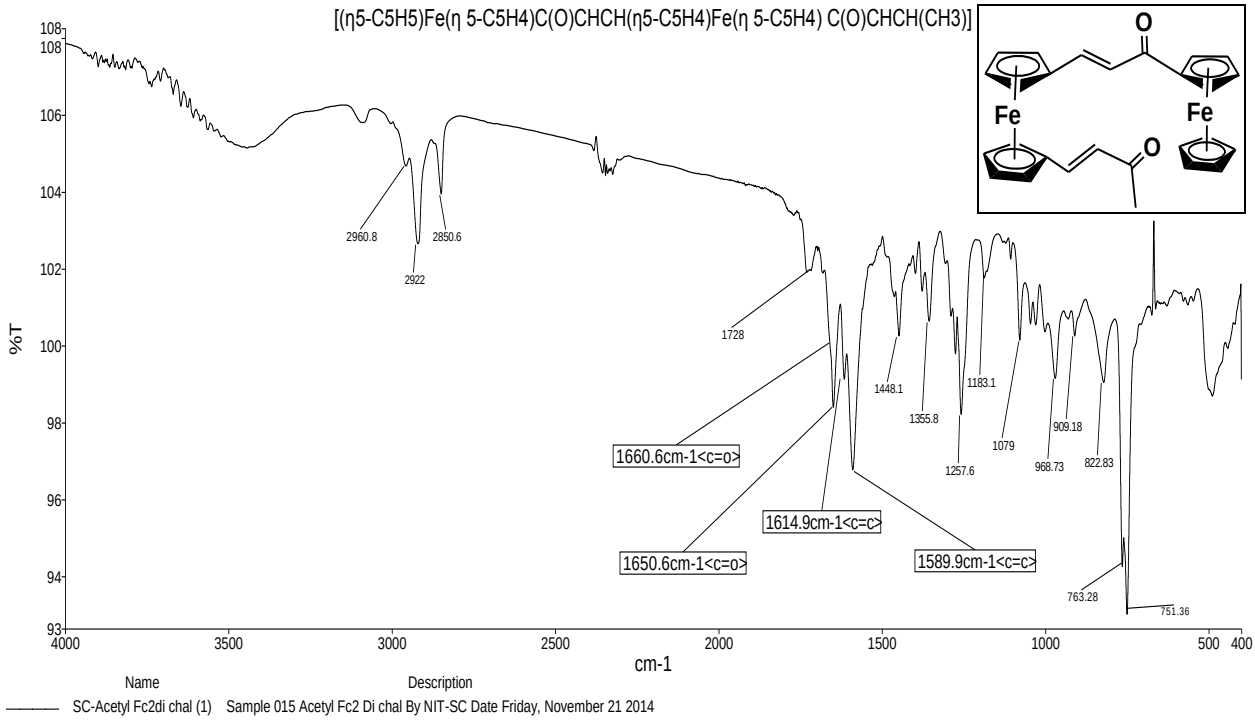
b) IR OF $[Fe_2(\eta^5\text{-}C_5H_4)_4\{(CHCH)C(O)\}_2]$:



c) IR OF [(η5-C5H5)Fe(η 5-C5H4)C(O)CHCH(η5-C5H4)Fe(η 5-C5H4) C(O)CHCH(ArOH)]:

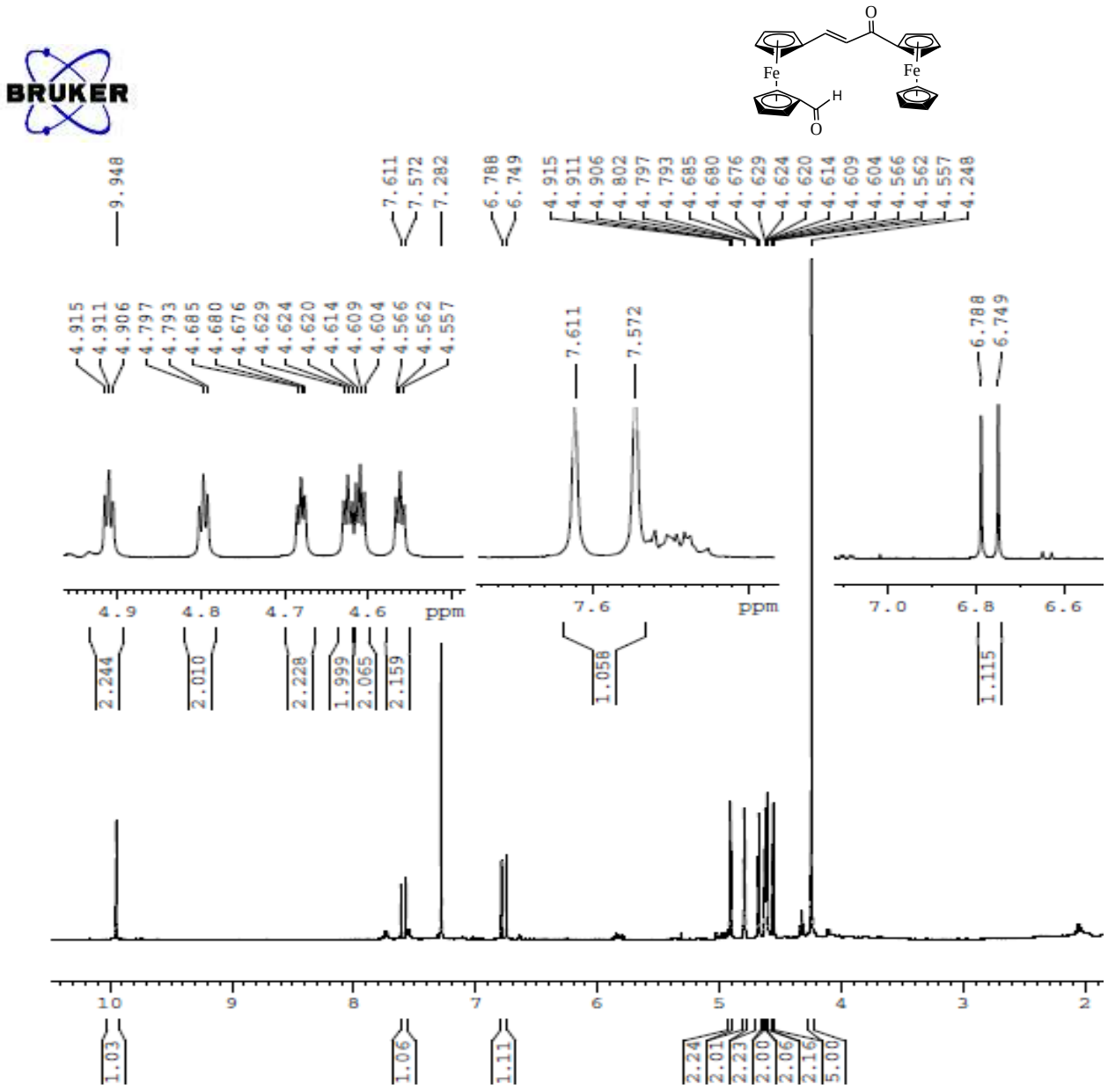


d)IR OF [(η5-C5H5)Fe(η 5-C5H4)C(O)CHCH(η5-C5H4)Fe(η 5-C5H4) C(O)CHCH(CH_3)]:

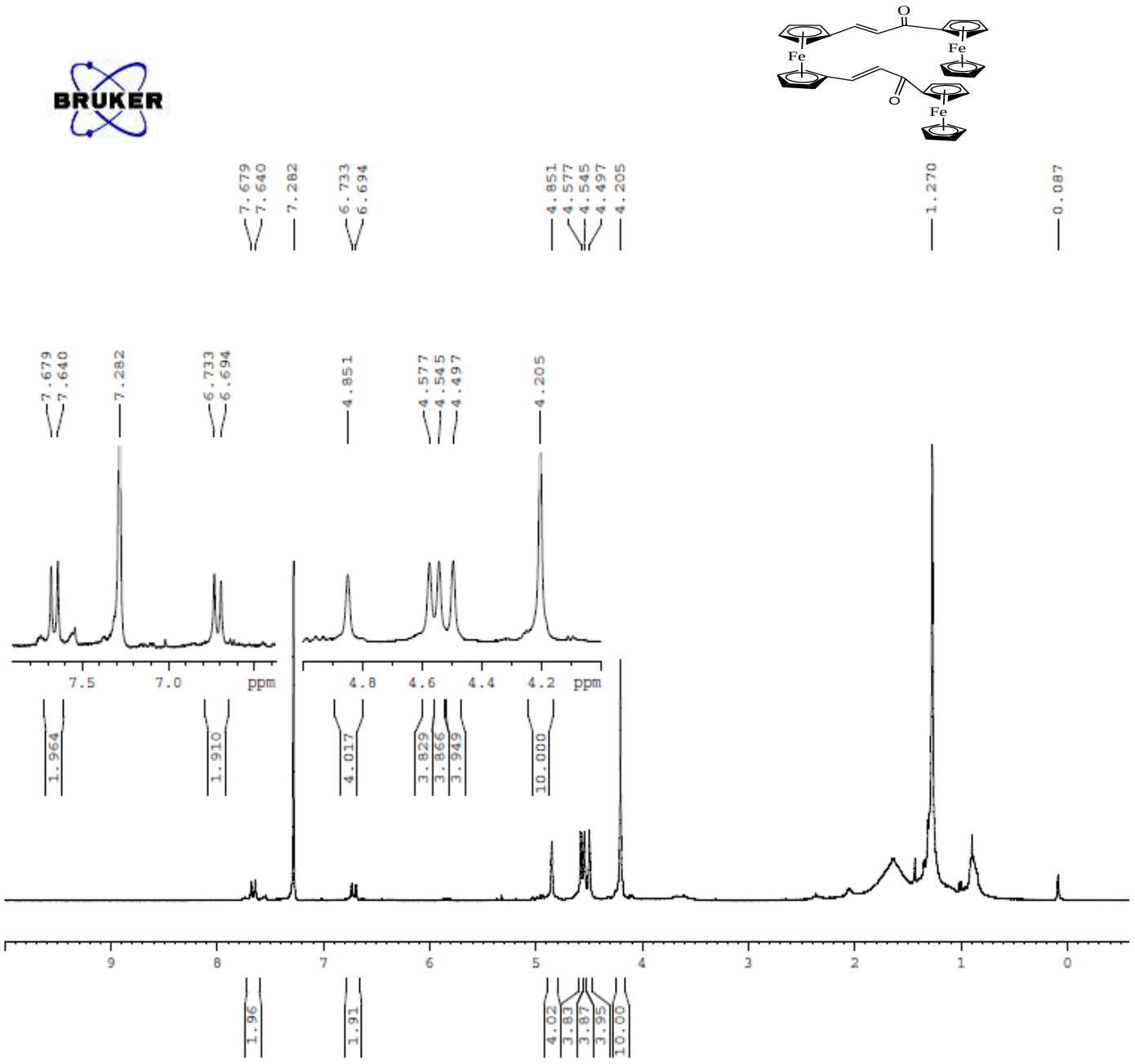


ANNEXURE 2:

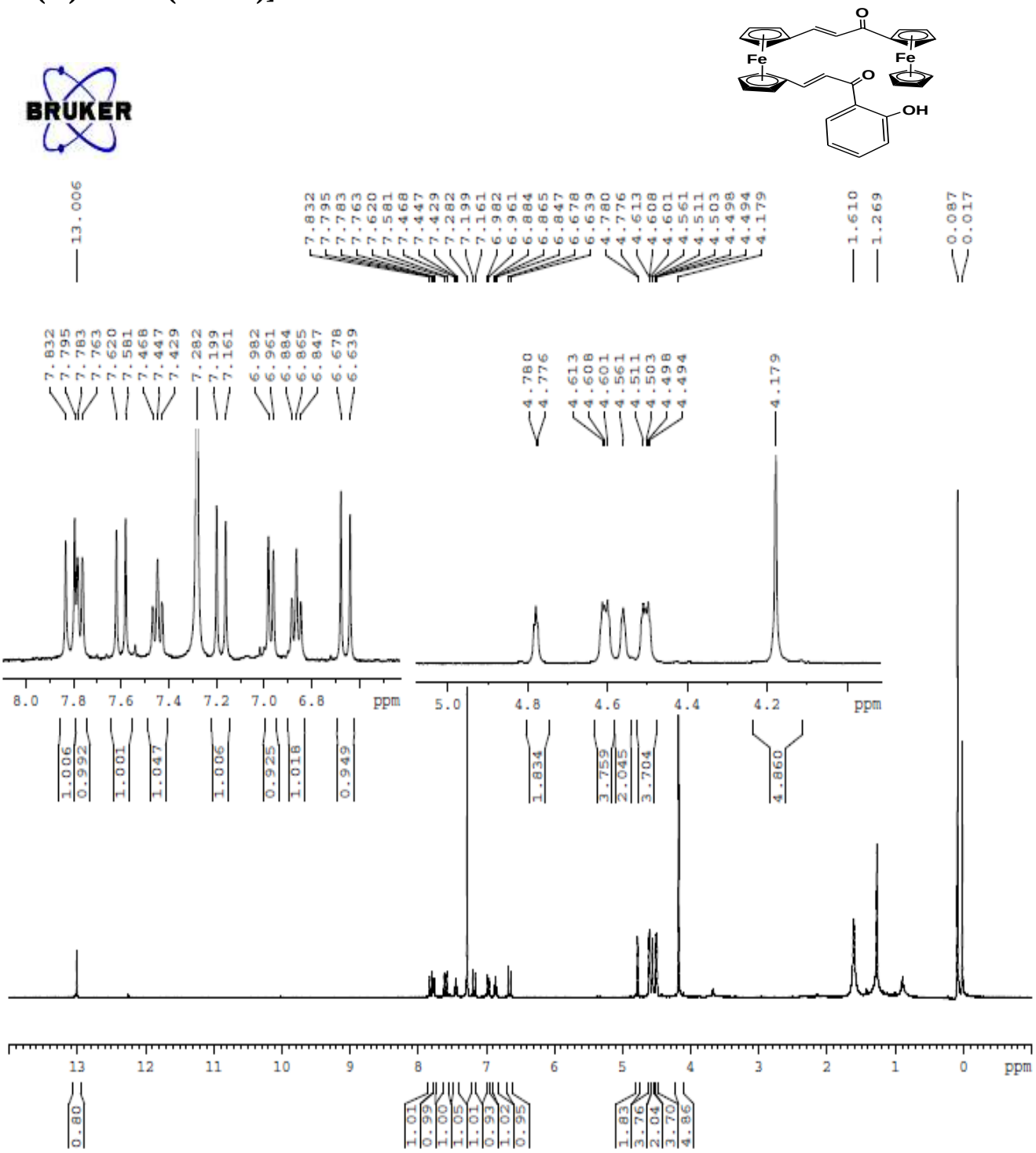
a)NMR OF [(η5-C5H5)Fe(η 5-C5H4)C(O)CHCH(η5-C5H4)Fe(η 5-C5H4)CHO]:



b) NMR OF $[Fe_2(\eta^5\text{-}C_5H_4)_4\{(CHCH)C(O)\}_2]$:



c)IR OF [(η5-C5H5)Fe(η 5-C5H4)C(O)CHCH(η5-C5H4)Fe(η 5-C5H4) C(O)CHCH(ArOH)]:



d)NMR OF [(η5-C5H5)Fe(η 5-C5H4)C(O)CHCH(η5-C5H4)Fe(η 5-C5H4) C(O)CHCH(CH_3)]: